



Group 1 ITI Consensus Report: The influence of implant length and design and medications on clinical and patient-reported outcomes

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Abstract: **OBJECTIVES:** The aim of Working Group 1 was to address the influence of different local (implant length, diameter, and design) and systemic (medications) factors on clinical, radiographic, and patient-reported outcomes in implant dentistry. Focused questions on (a) short posterior dental implants (6 mm), (b) narrow diameter implants, (c) implant design (tapered compared to a non-tapered implant design), and (d) medication-related dental implant failures were addressed. **MATERIALS AND METHODS:** Four systematic reviews were prepared in advance of the Consensus Conference and were discussed among the participants of Group 1. Consensus statements, clinical recommendations, and recommendations for future research were based on structured group discussions until consensus was reached among the entire expert Group 1. The statements were then presented and accepted following further discussion and modifications as required by the plenary. **RESULTS:** Short implants (6 mm) revealed a survival rate ranging from 86.7% to 100%, whereas standard implant survival rate ranged from 95% to 100% with a follow-up from 1 to 5 years. Short implants demonstrated a higher variability and a higher Risk Ratio [RR: 1.24 (95% CI: 0.63, 2.44, $p = 0.54$)] for failure compared to standard implants. Narrow diameter implants (NDI) have been classified into three categories: Category 1: Implants with a diameter of <2.5 mm ("Mini-implants"); Category 2: Implants with a diameter of 2.5 mm to <3.3 mm; Category 3: Implants with a diameter of 3.3 mm to 3.5 mm. Mean survival rates were $94.7 \pm 5\%$, $97.3 \pm 5\%$ and $97.7 \pm 2.3\%$ for category 1, 2 and 3. Tapered versus non-tapered implants demonstrated only insignificant differences regarding clinical, radiographic, and patient-reported outcomes. The intake of certain selective serotonin reuptake inhibitors and proton pump inhibitors is associated with a statistically significant increased implant failure rate. The intake of bisphosphonates related to the treatment of osteoporosis was not associated with an increased implant failure rate. **CONCLUSIONS:** It is concluded that short implants (6 mm) are a valid option in situations of reduced bone height to avoid possible morbidity associated with augmentation procedures; however, they reveal a higher variability and lower predictability in survival rates. Narrow diameter implants with diameters of 2.5 mm and more demonstrated no difference in implant survival rates compared to standard diameter implants. In contrast, it is concluded that narrow diameter implants with diameters of less than 2.5 mm exhibited lower survival rates compared to standard diameter implants. It is further concluded that there are no differences between tapered versus non-tapered dental implants. Certain medications such as selective serotonin reuptake inhibitors and proton pump inhibitors showed an association with a higher implant failure rate.

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Group 1 ITI Consensus Report: The influence of implant length and design and medications on clinical and patient-reported outcomes

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Abstract

Objectives: The aim of Working Group 1 was to address the influence of different local (implant length, diameter, and design) and systemic (medications) factors on clinical, radiographic, and patient-reported outcomes in implant dentistry. Focused questions on (a) short posterior dental implants (≤ 6 mm), (b) narrow diameter implants, (c) implant design (tapered compared to a non-tapered implant design), and (d) medication-related dental implant failures were addressed.

Materials and methods: Four systematic reviews were prepared in advance of the Consensus Conference and were discussed among the participants of Group 1. Consensus statements, clinical recommendations, and recommendations for future research were based on structured group discussions until consensus was reached among the entire expert Group 1. The statements were then presented and accepted following further discussion and modifications as required by the plenary.

Results: Short implants (≤ 6 mm) revealed a survival rate ranging from 86.7% to 100%, whereas standard implant survival rate ranged from 95% to 100% with a follow-up from 1 to 5 years. Short implants demonstrated a higher variability and a higher Risk Ratio [RR: 1.24 (95% CI: 0.63, 2.44, $p = 0.54$)] for failure compared to standard implants.

Narrow diameter implants (NDI) have been classified into three categories: Category 1: Implants with a diameter of < 2.5 mm ("Mini-implants"); Category 2: Implants with a diameter of 2.5 mm to < 3.3 mm; Category 3: Implants with a diameter of 3.3 mm to 3.5 mm. Mean survival rates were $94.7 \pm 5\%$, $97.3 \pm 5\%$ and $97.7 \pm 2.3\%$ for category 1, 2 and 3. Tapered versus non-tapered implants demonstrated only insignificant differences regarding clinical, radiographic, and patient-reported outcomes.

The intake of certain selective serotonin reuptake inhibitors and proton pump inhibitors is associated with a statistically significant increased implant failure rate. The intake of bisphosphonates related to the treatment of osteoporosis was not associated with an increased implant failure rate.

Conclusions: It is concluded that short implants (≤ 6 mm) are a valid option in situations of reduced bone height to avoid possible morbidity associated with augmentation procedures; however, they reveal a higher variability and lower predictability in survival rates. Narrow diameter implants with diameters of 2.5 mm and more demonstrated no difference in implant survival rates compared to standard diameter implants. In contrast, it is concluded that narrow diameter implants with diameters of less than 2.5 mm exhibited lower survival rates compared to standard diameter implants. It is further concluded that there are no differences between tapered versus non-tapered dental implants. Certain medications such as selective serotonin reuptake inhibitors and proton pump inhibitors showed an association with a higher implant failure rate.

KEYWORDS

biological complications, clinical decision-making, dental implants, drug, endosseous implant, epidemiology, failure, humans, medication, meta-analysis, narrow diameter, osteotomy, randomized controlled trials, review, short dental implants, small dental implants, survival

1 | INTRODUCTION

The objectives of Group 1 of the 6th ITI Consensus Conference were to provide statements and recommendations for clinicians and researchers related to short implants (≤ 6 mm), narrow diameter implants (≤ 3.5 mm), implant designs (tapered versus non-tapered), and certain medications on clinical, radiographic, and patient-reported outcomes in implant dentistry.

For Working Group 1, four systematic reviews have been prepared and reviewed before the Consensus Conference. Based on the data and the meta-analysis of the individual, systematic reviews and basis on thorough discussions among the participants of Group 1 and among the entire plenum of the conference consensus statements and clinical recommendations were carefully formulated. In addition, recommendations for future research were also prepared by the working group. The four systematic reviews are listed below:

1. Survival rates of short dental implants (≤ 6 mm) compared with implants longer than 6 mm in posterior jaw areas: A meta-analysis.
Panos Papaspyridakos, Andre De Souza, Konstantinos Vazouras, Hadi Gholami, Sarah Pagni, Hans-Peter Weber
2. Narrow diameter implants: A systematic review and meta-analysis
Eik Schiegnitz, Bilal Al-Nawas
3. Systematic review of clinical and patient-reported outcomes following oral rehabilitation on dental implants with a tapered compared to a non-tapered implant design
Asbjørn Jokstad, Jeffrey Ganeles
4. Medication-related dental implant failure: Systematic review and meta-analysis
Vivianne Chappuis, Gustavo Avila-Ortiz, Mauricio Araújo, Alberto Monje

2 | SURVIVAL RATES OF SHORT DENTAL IMPLANTS (≤ 6 MM) COMPARED WITH IMPLANTS LONGER THAN 6 MM IN POSTERIOR JAW AREAS: A META-ANALYSIS

2.1 | Preamble

Short implants have been proposed as an alternative to eliminate or reduce the need for vertical bone augmentation procedures, which are often associated with additional costs, longer treatment time,

increased postoperative morbidity, and greater risk for complications. However, the long-term efficacy of short dental implants has been a topic of controversy in the dental implant literature. Whereas some studies reported lower survival rates for short compared to longer implants, other reports, including a number of systematic reviews, more recently concluded that survival rates of short implants are similar to longer implants placed in pre-existing or grafted bone. The majority of studies does not include direct comparisons of the performance of short and longer implants. The interpretation of the literature is also complicated by the fact that authors have defined "short dental implants" differently. Some have considered <10 mm as short, whereas in other studies, short implants were 8 mm or less, 7 mm or less, or 6 mm or less.

The purpose of this study was to systematically review randomized controlled clinical trials (RCTs) reporting on long-term survival as well as complication rates of short implants (≤ 6 mm) versus longer implants (>6 mm) in posterior jaw areas of partially edentulous patients.

The main goal and primary outcome of this systematic review and meta-analysis was to compare long-term survival rates between short implants (≤ 6 mm) and longer implants (>6 mm) in posterior jaw areas.

Secondary outcomes were as follows:

- Radiographic bone levels
- Prosthesis survival
- Implant complications

The present systematic review is based on 10 randomized clinical trials including 775 patients (392 with short and 383 with longer implants) representing a total of 1,290 implants (637 short and 653 longer implants). The follow-up period ranged from 1 to 5 years.

Sufficient data were available to perform a meta-analysis of the primary outcome (implant survival). Only descriptive analyses were possible for the secondary outcomes radiographic bone levels, prosthesis survival, and biologic complication rates for implants.

When interpreting the results, it is important to realize that only three of the 10 studies evaluated the performance of short and longer implants in a randomized manner in sites allowing the placement of both types of implants. The other seven studies compared the use of short implants to longer implants in conjunction with augmentation procedures. In other words, these seven studies compare different treatment approaches and not necessarily implant lengths per se. This difference needs to be kept in mind when comparing the results of these studies.

2.2 | Consensus statements

2.2.1 | Consensus statement 1

Short implants (≤ 6 mm) exhibit similar survival rates compared to longer implants (> 6 mm) after periods of 1–5 years in function. The mean survival rate was 96% (range: 86.7%–100%) for short implants, and 98% (range 95%–100%) for longer implants. The meta-analysis showed a risk ratio of 1.29 (95% CI: 0.67, 2.50, $P = 0.45$) for failure when short implants were used.

This statement is based on a meta-analysis of 10 RCTs including 775 patients (392 patients with short, 383 with longer implants) and 1,290 implants (637 short, 653 longer implants).

2.2.2 | Consensus statement 2

Time in function may reduce the survival rate of short implants more than that of longer implants.

This statement is based on one RCT with a follow-up of 5 years including 45 patients and 60 implants (30 short, 30 longer). This is additionally confirmed by a recently published RCT with a 5-year patient follow-up that could not be included as it was published after the cut-off date for inclusion in the systematic review.

2.2.3 | Consensus statement 3

Short and longer implants present similar amounts of radiographic interproximal bone level changes. Following a period of 1–5 years, the radiographic interproximal bone level changes for the short implants ranged from +0.06 to −1.22 mm, whereas the corresponding values for the longer implants ranged from +0.02 to −1.54 mm.

This statement is based on 10 RCTs including 775 patients (392 patients with short, 383 with longer implants) and 1,290 implants (637 short, 653 longer implants).

2.2.4 | Consensus statement 4

The rate of surgical and postsurgical complications is higher in the longer implant group (mean: 32.8%; range: 0–90%) compared to the short implants (mean: 6.8%; range: 0–26%).¹ In the longer implant group, the majority of complications were associated with bone grafting procedures.²

2.2.5 | Consensus statement 5

Prosthesis survival for short and longer implants following a period of 1–5 years is similarly high. The mean prosthesis survival rate was

98.6% (range: 90%–100%) for the short implants, and 99.5% (range: 95%–100%) for the longer implants.

This statement is based on nine RCTs including 625 patients (317 patients with short and 308 with longer implants).

2.3 | Clinical recommendations

2.3.1 | What are the current indications for short implants?

Short implants are a valid option in situations of reduced bone height when it is important to avoid possible morbidity associated with augmentation procedures or to reduce treatment time. They may also be preferred when the possibility of damage to adjacent structures can be significantly reduced. Adjacent structures include maxillary sinuses, blood vessels and nerves, tooth structures and existing implants.

2.3.2 | Should longer implants be the first choice?

The selection of the length of an implant depends on site-specific local anatomical and patient conditions. When sufficient bone height exists, implants longer than 6 mm are preferred when they can be placed without increasing surgical risk.

2.3.3 | Can short implants be immediately loaded?

The loading times for short implants reported in the literature ranged from 6 weeks to 6 months. At the present time, no evidence-based recommendation can be made for immediate loading.

2.3.3 | Does implant diameter affect the survival of short implants?

Based on the findings from the studies included in this review, short implants with a diameter of 4 mm or greater should be used.

2.3.4 | Should adjacent short implants be splinted?

Based on the findings from the studies included in this review, the clinical recommendation is made to splint restorations involving adjacent short implants.

2.3.5 | What are the occlusal considerations for restorations on short implants?

Although the reviewed literature does not give specific recommendations regarding occlusion, a greater risk of occlusal overload of short implants has to be considered. Caution is especially advised when indicating short implants in patients presenting with single missing molars and/or parafunctional habits. Changes in occlusion should be assessed and adjusted as necessary during regular maintenance visits.

¹This statement is based on eight RCTs including 590 patients (298 patients with short, 292 with longer implants) having 1,022 implants (500 short, 522 longer implants).

²This statement is based on six RCTs including 305 patients (134 patients with short and 171 with longer implants) and confirms previous consensus reports.

2.4 | Recommendations for future research

- Prospective long-term clinical studies on the performance of short implants (>5 years)
- Randomized clinical trials comparing short and longer implants in intact bone sites without the need for vertical bone augmentation.
- RCTs or long-term controlled clinical studies on the effect of splinting
- Studies on optimal implant design for short implants

3 | NARROW DIAMETER IMPLANTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

3.1 | Preamble

Narrow diameter implants (NDI) are used in clinical situations including narrow bony ridges as an alternative to bone augmentation procedures and in sites with reduced interdental gap width. The aim of the systematic review was to assess the survival rates of NDI made from titanium or titanium alloy and to provide recommendations and guidelines for the application of NDI.

There is a need for clarity and standardization in the description of the diameter of an implant. For the purpose of this study, the maximal endosseous implant diameter has been used, including implant threads, as provided by the implant manufacturer. The available literature describes the use of different types of NDI, but it appears generally accepted that a NDI is one with a diameter of ≤ 3.5 mm.

Since the previous classification of NDI (Klein, Schiegnitz, & Al-Nawas, 2014), there have been new developments in the field of NDI and therefore, the following modification to this classification is proposed:

Category 1: Implants with a diameter of <2.5 mm ("Mini-implants")

Category 2: Implants with a diameter of 2.5 mm to <3.3 mm

Category 3: Implants with a diameter of 3.3 mm to 3.5 mm

At the present time, most implants of <2.5 mm diameter are one-piece implants. One-piece implants with a diameter of >3.0 mm are rarely described.

From 5,845 records retrieved initially, 72 studies were included in the qualitative analysis and 16 studies in the quantitative analysis. Quality assessment of the included literature showed considerable variation, with a high risk of bias. It should be noted that important aspects relating to clinical outcomes are not reported: There are no data on patient-reported outcome measures, loading protocols, biological or technical complications, all of which could impact on the actual clinical performance and longevity of the provided treatment.

It is important to note that there are no studies comparing NDI without bone augmentation procedures to SDI with bone augmentation procedures.

3.2 | Consensus statements

3.2.1 | Consensus statement 1

Mean survival rate of Category 1 implants was $94.5\% \pm 5\%$ (Range 80%–100%) after observation periods of 12–78 months. The most frequently described applications of these implants were for transitional restorations, overdentures, and single anterior tooth replacement.

This statement is based on 20 clinical trials (eight RS, 10 PS, and two RCTs) with 1,220 patients and 5,367 implants. The majority of the included papers exhibited a high risk of bias.

3.2.2 | Consensus statement 2

Mean survival rates of Category 2 implants were $97.3\% \pm 4\%$ (Range 80.5%–100%) after observation periods of 12–63 months. The most frequently described application was for single anterior tooth replacement.

This statement is based on 21 clinical trials (10 RS, 9 PS, and 2 RCTs) with 883 patients and 1,207 implants. The majority of the included papers exhibited a high risk of bias.

Compared to SDI, Category 2 NDI exhibit comparable survival rates in meta-analysis ([OR], 1.06; [CI], 0.31–3.61). This statement is based on four clinical trials (2 RS, 1 PS, and 1 RCT). The majority of the included papers exhibited a high risk of bias.

3.2.3 | Consensus statement 3

Mean survival rates of Category 3 implants were $97.7\% \pm 2\%$ (Range 91%–100%) after observation periods of 12–109 months. The applications of these implants were not always precisely defined, but also included the replacement of posterior teeth in either arch.

This statement is based on 35 clinical trials (17 RS, 12 PS, and six RCT) with 3,842 patients and 5,612 implants. The majority of the included papers exhibited a high risk of bias.

Compared to SDI, Category 3 NDI exhibit comparable survival rates in meta-analysis ([OR], 1.19; [CI], 0.83–1.70). This statement is based on 10 clinical trials (eight RS, and two RCT). The majority of the included papers exhibited a high risk of bias.

3.2.4 | Consensus statement 4

There is insufficient evidence on the success rates for all NDIs. Clinical parameters and treatment protocols are often not sufficiently described and no controlled comparative long-term studies are available, resulting in a high risk of bias.

3.3 | Clinical recommendations

3.3.1 | What are the potential advantages of using NDI?

- NDI should be considered when it is important to ensure maintenance of adequate tooth-implant and implant-implant distances in

sites with reduced mesio-distal width.

- The use of NDI can be considered to reduce the need or complexity of lateral bone augmentation procedures to reduce morbidity.
- The use of NDI may allow simultaneous rather than staged bone augmentation procedures.
- The use of NDI may provide increased prosthetic flexibility in certain clinical situations.

3.3.2 | What are the potential disadvantages of using NDI?

Biological

- One-piece NDI with ball attachments might be difficult to manage at the onset of dependency.
- The use of NDI may compromise optimal prosthetic designs allowing the maintenance of peri-implant tissue health.

Mechanical

- Reducing implant diameter brings an increased risk of implant or component fracture.
- Caution is recommended for the use of NDI in patients with para-functional habits and malocclusions.

3.3.3 | Should NDI be splinted?

Given the reduced implant strength and bone contact offered by NDI, it may be advisable to use splinted restorations based on the individual clinical situation.

3.3.4 | What are the indications for each classification of NDI?

Category 1 implants can be considered for:

- Support of definitive complete mandibular overdentures
- Support of interim prostheses, both fixed and removable

Category 2 implants can be considered for:

- Support of definitive complete mandibular overdentures
- Support of single tooth replacement in the anterior zone with narrow interdental width (maxillary lateral incisors and single mandibular incisors)

Category 3 implants can be considered for:

- Support of definitive complete overdentures
- Support of single tooth replacement in sites with reduced interdental and/or buccal-lingual width
- Support of multiple unit restorations

Personalized informed consent should include the possibility of more technical and biological complications.

3.4 | Recommendations for future research

- Future studies should compare the success and patient-reported outcome measures between NDI without augmentation procedure and SDI with an augmentation procedure.
- Future studies should document long-term results of potential technical and biological complications
- Future studies should compare new materials and implant designs.
- Future studies should investigate the aesthetic outcome of NDI.

4 | SYSTEMATIC REVIEW OF CLINICAL AND PATIENT-REPORTED OUTCOMES FOLLOWING ORAL REHABILITATION ON DENTAL IMPLANTS WITH A TAPERED COMPARED TO A NON-TAPERED IMPLANT DESIGN

4.1 | Preamble

Approximately 50% of all implants on the market are tapered. In this systematic review, a tapered implant is recognized as a cylindrical implant where the endosseous part narrows in diameter toward the apex. The rationale for using this implant design is to improve primary stability and subsequent treatment success.

The present systematic review evaluated the scientific evidence related to implant survival and success to address the question: In patients with dental implant restorations, do tapered compared to non-tapered implants demonstrate similar clinical and patient-reported outcomes?

Twenty-nine articles were identified of which three RCTs reported outcomes at 3 years. The three RCTs described the results of 245 patients with 388 implants at three years and reported clinically insignificant differences. The three RCTs each reported different clinical outcomes and the data were not comparable. None reported patient-reported outcomes or maintenance needs. All three RCTs have a moderate risk of bias. Meta-analyses were not conducted.

4.2 | Consensus statements

4.2.1 | Consensus statement 1

The evidence shows that both tapered and non-tapered implants demonstrate satisfactory performance with respect to marginal bone levels at 3 years. This statement is based on the evidence of three RCTs, (245 patients with 388 implants).

4.2.2 | Consensus statement 2

There is currently insufficient evidence to conclude if tapered compared with non-tapered implants demonstrate similar clinical and

patient-reported outcomes. This statement is based on the evidence from three RCTs, (245 patients with 388 implants).

4.3 | Clinical recommendations

4.3.1 | Is there a recommendation for any specific implant design with regard to taper?

Based on Consensus statements 1 and 2, both tapered and non-tapered implants can be used according to the operator's preference.

4.3.2 | Are there particular clinical situations in which any specific implant design with regard to taper is preferred?

Tapered implants can be considered in clinical situations to avoid injuring anatomical structures or causing apical fenestrations.

Appropriate professional judgment and clinical decision-making must include a comprehensive diagnosis of the patient's jawbone anatomy, bone quality and quantity, and osteotomy protocol.

4.3.3 | Is utilizing a tapered implant an effective strategy to increase insertion torque?

In situations where increased insertion torque is desired, tapered implants may be considered. The shape of the dental implant is only one contributing factor to achieve high insertion torque; however, the clinical significance of implant shape on long-term results is unclear.

4.4 | Recommendations for future research

- Clinically validate a nomenclature and classification system to describe and compare different configurations of "tapered" implants (Figure 1).
- Clinical studies that aim to compare tapered versus non-tapered implant designs should include details of bone quality and quantity, the osteotomy preparation protocols, (osteotomy shape, degree of under sizing, method of osteotomy (twist drill, piezo, condensation, etc.)).

- Establish whether insertion torque and resonance frequency analysis are valid indicators of the risk of micromotion as a function of the implant design.

5 | MEDICATION-RELATED DENTAL IMPLANT FAILURE: A SYSTEMATIC REVIEW AND META-ANALYSIS

5.1 | Preamble

Current global trends indicate that the general population's expectancy of life is increasing worldwide. These demographic changes have been associated with an increase in the intake of medications for the treatment of highly prevalent medical conditions. Some of these medications may influence tissue metabolism and, therefore, the outcomes of implant therapy in certain cohorts. Interestingly, the impact of medication that may particularly alter bone homeostasis upon implant therapy outcomes has not been systematically explored.

The main goal of this systematic review was to assess the association of implant failure rate as the primary outcome with intake of oral or parenteral medications that may affect bone metabolism.

Secondary outcomes were:

- Timing of implant failure.
- Marginal bone loss.
- Biological and Mechanical/Technical complications.

The present systematic review includes 17 investigations, one CCT had to be excluded due to missing reports on implant failures rates. The 16 remaining studies consisted of three RCTs, one PC and 12 RC including a total of 4,827 patients with 13,247 implants.

A total of five different categories of medications were identified upon completion of the systematic search: nonsteroidal anti-inflammatory medication (NSAIDs), antihypertensive medication (AHTNs), selective serotonin reuptake inhibitors (SSRIs), proton pump inhibitors (PPIs), and bisphosphonates (BPs). Sufficient data were available to perform meta-analyses of the primary outcomes for SSRIs, PPIs, and BPs. The heterogeneity of the study design and methodology in the selected studies did not allow for meta-analyses for any of the secondary outcomes. Limitation of this systematic

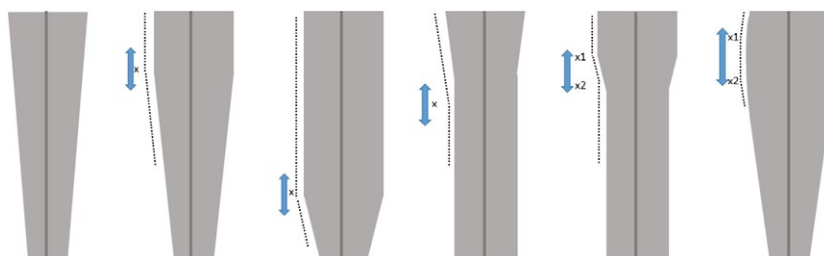


FIGURE 1 Different types of configurations and geometrie for tapered implants available on the dental market

review is related to differences in study design and medication regimens, in addition to confounding factors, such as comorbidity and polypharmacy among others reported in the literature. Therefore, the findings of this systematic review should be interpreted with caution.

5.2 | Consensus statements

5.2.1 | Consensus statement 1: General Statement

Limited evidence on the effect of long- and short-term medication intake on dental implant therapy outcomes indicates that there may be an association between implant failure rate and the intake of certain medications that influence bone metabolism.

5.2.2 | Consensus statement 2: nonsteroidal anti-inflammatory drugs (NSAIDs)

The association between nonsteroidal anti-inflammatory drug (NSAID) intake and implant failure rate is unclear.

This statement is based on the analysis of five studies (i.e., three RCTs, including a total of 191 patients, and two retrospective cohort studies, including a total of 81 patients) that revealed marked heterogeneity of the pharmacological regimen in the selected studies and a majority of studies reporting no implant failures in either the test or control groups, or both groups.

i.e., Ibuprofen, Flurbiprofen, Celecoxib, Acetylsalicylic, Rofecoxib, Nabumetone, Naproxen, Etodolac and others.

5.2.3 | Consensus statement 3: antihypertensive medication (AHTNs)

The association between the long-term intake of certain AHTNs and implant failure rate is unclear.

This statement is based on very limited available evidence of one retrospective study including 728 patients. Noteworthy, AHTNs exhibited a lower implant failure rate compared to the control population not taking AHTNs in this study.

i.e., Beta-blockers, Thiazide diuretics, Angiotensin-converting enzyme inhibitors, Angiotensin II receptor blockers and others.

5.2.4 | Consensus statement 4: selective serotonin reuptake inhibitors (SSRIs)

The intake of certain SSRIs is associated with a statistically significant increased implant failure rate.

This statement is based on the quantitative analysis of two retrospective cohort studies including a total of 790 patients, which suggested that implant failure rate was higher in subjects taking SSRIs as compared to a control population (Odds ratio: 2.92; average difference: 7.48%, C.I. [95%] = 6.96–8.00 with a $p < 0.01$, between 36 and 90 months of follow-up).

i.e., Citalopram, Dapoxetine, Escitalopram, Fluoxetine, Fluvoxamine, Indalpine, Paroxetine, Sertraline, Venlafaxine and Zimeline and others.

5.2.5 | Consensus statement 5: proton pump inhibitors (PPIs)

The intake of PPIs is associated with a statistically significant increased implant failure rate.

This statement is based on the quantitative analysis of two retrospective cohort studies including a total of 1,798 patients, which suggested that implant failure rate was higher in subjects taking PPIs as compared to a control population (Odds ratio: 2.02; average difference: 4.29%, C.I. [95%] = 3.81–4.77 with a $p < 0.01$, between 16 and 94 months of follow-up).

i.e., Omeprazole, Lansoprazole, Pantoprazole, Dexlansoprazole, Esomeprazole, Rabeprazole and others.

5.2.6 | Consensus statement 6: bisphosphonates (BPs) related to osteoporosis

The intake of BPs related to the treatment of osteoporosis was not associated with an increased implant failure rate.

This statement is based on the quantitative analysis of six cohort studies (i.e., five retrospective on oral BPs and one prospective using intravenous BPs including a total of 1,239 patients), which suggested that implant failure rate was higher in subjects taking BPs as compared to a control population (average difference: -0.13%, C.I. [95%] = -0.3 to 0.05, between 12 and 66 months of follow-up). Caution should be taken when interpreting these data due to the inherent risks associated with the occurrence of medication-induced osteonecrosis in patients taking BPs.

The effect of BP on implant outcomes in patients undergoing treatment of neoplastic diseases therapy was not evaluated, because implant therapy is usually contraindicated in this population.

i.e., Risedronate, Ibandronate, Alendronate, Zoledronic acid and others.

5.3 | Clinical recommendations

5.3.1 | What are the implications of the increasing intake of medication by the general population in daily practice?

Clinicians and patients considering implant therapy should be aware of possible medication-related implant failures. Hence, a comprehensive assessment and understanding of the patient's medical background and current medications, as well as a personalized informed consent, should be considered integral components of all phases of contemporary implant therapy (initial and supportive therapy).

5.3.2 | What considerations should be taken in daily clinical practice pertaining medication intake-related implant failure?

Clinicians should consider the association between increased implant failure rate and the intake of proton pump inhibitors (PPIs) or selective serotonin reuptake inhibitors (SSRIs) in their routine risk assessment as part of comprehensive implant therapy.

Clinicians should proceed with caution when implant therapy is considered in patients taking bisphosphonates (BPs) related to osteoporosis.

Standard implant therapy is contraindicated in patients receiving high-dose bisphosphonates (BPs) for the treatment of neoplastic diseases.

5.4 | Recommendations for future research

- To elucidate potential mechanisms of action that would explain the effect of certain medications on bone and soft tissue homeostasis around implants exhibiting different macro- and microscopic features via the conduction of *in vivo* preclinical studies.
- To investigate potential cause–effect relationships between the intake of certain medications and implant outcomes through prospective clinical trials evaluating clinical, radiographic, microbiological, histological, PROMs, and other parameters. This will expand our knowledge and increase the success of implant therapy.

- To evaluate the effect of confounders, such as the disease itself, comorbidities, behavioral aspects, and polypharmacy, on implant therapy outcomes in prospective clinical trials including target populations.

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